Remarks

Status of the Claims

Pending claims

Claims 2 to 14, 16 to 20, 22 and 44 to 60 are pending and under consideration. Claims 45, 53, 54, 56, and 57 are amended herein. Applicants respectfully submit that these amendments simply to correct typographical errors and clarify the language used to claim Applicants' pioneering invention, and are not being made for purposes of patentability. Claims 1, 15, 21, 23 to 42 and 43 were canceled in the amendment submitted July 12, 2001.

Outstanding Rejections

Claims 2 to 14, 16 to 20, 22 and 44 to 60 stand rejected under 35 USC §112, second paragraph. Claims 2 to 14, 16 to 20, 22, 53, and 57 stand rejected under 35 U.S.C. §101. Claims 2 to 14, 16 to 20, 22 and 44 to 60 stand rejected under 35 USC §102(b) as allegedly anticipated by, or, in the alternative, under 35 USC §103(a) as allegedly unpatentable over Wallace, et al. (1996) Protein Science 5:1001-1013. Claims 2 to 14, 16 to 20, 22 and 44 to 60 stand rejected under 35 USC §102(b) as allegedly anticipated by Holm, et al. (1997) PROTEINS: Structure, Function and Genetics 28:72-82. Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Interview with Examiner

Applicants respectfully request an interview with the Examiner before the first examination on the merits for this RCE.

Support for the Claim Amendments

The specification sets forth an extensive description of Applicants' claimed pioneering invention. Support for the instant amendments can be found specifically, for example, at specification page 23, lines 23-30, which reads:

"In preferred embodiments, the said one or more atoms is selected from the group consisting of amide nitrogens, a-carbons, carbonyl carbons, and carbonyl oxygens within a polypeptide backbone, b-carbons of amino acid residues, and pseudoatoms." Id., emphasis added.

See also specification pages 24-25, which read as follows:

"In many embodiments, all of the atoms for which geometric constraints are provided comprise a part of the polypeptide backbone and are selected from the group consisting of a-carbons, amide nitrogens, carbonyl carbons, and carbonyl oxygens. Of course, one or more of such atoms can be a pseudoatom. Representative examples of pseudoatoms are centers of mass, such as may be derived from at least two atoms, such as two or more atoms from one amino acid residue or two or more atoms from at least two amino acid residues of the protein." Id., page 24, line 29 – page 30, line 7.

Objections to the disclosure

The disclosure has been objected to because it contains imbedded hyperlinks. MPEP §608.01(b). Applicants will address this objection upon receipt of a notice of allowable subject matter.

Issues under 35 U.S.C. §112, second paragraph

Claims 2 to 14, 16 to 20, 22 and 44 to 60 stand rejected under 35 USC §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "first amino acid"

In claim 53 the term "first amino acid" appears twice, in item (a) and then in item (b)(i). Clarification as to whether the term "first amino acid" in (a) and (b)(i) is the same amino acid has been requested.

Item (a) reads: "(a) an amino acid residue identity constraint for a first amino acid residue of the functional site, wherein the first amino acid residue is identified as a single amino residue or as a subset of amino acid residues;" (emphasis added)

Item (b)(i) reads: "(i) an atom of the first amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a

backbone carbonyl oxygen, a backbone pseudoatom and a beta-carbon;"

(emphasis added)

Applicants confirm that the "first amino acid" in both limitations is the same "first amino acid." Antecedent basis for "the first amino acid" (a first amino acid) is found in item (a).

The term "third ... reside of the protein"

In claim 53, item (b)(iii), the term "third ... reside of the protein", is alleged to lack antecedent basis.

Antecedent basis for the term "the protein" is found in the preamble, which reads "A computer program product encoding a functional site descriptor, wherein the functional site descriptor defines at least one functional site of a protein, ..."

Antecedent basis for claims 15 and 44

The Patent Office notes that claims 15 and 44 lack antecedent basis because their base claims have been canceled. Applicants respectfully note that claim 15 was canceled in their July 12, 2001, response, whereas claim 44 depends on pending claim 54.

Issues under 35 U.S.C. §101

The rejection of claims 1 to 22 under 35 U.S.C. §101 has been maintained because the claimed invention is allegedly directed to non-statutory subject matter. Specifically, it is alleged that claims drawn to "functional site descriptors" and libraries of these descriptors are non-statutory subject matter.

Applicants respectfully aver that claim amendments have addressed this issue. Claim 1 has been canceled. Claims 2 to 22 depend directly or indirectly on claim 53, which is drawn to a computer program product. Computer program products and the like have been recognized as patentable subject matter by the Patent Office. See MPEP § 2106. As such, this objection should be withdrawn.

Claims 53, 2 to 14 (which depend directly or indirectly on claim 53) and 57 remain rejected under 35 U.S.C. §101 for allegedly being directed to non-statutory subject matter. The Patent Office alleges that a claim drawn merely to a computer program product is

non-statutory subject matter. In response to Applicants' reference to claim 8 of U.S. Patent No. 6,242,180, the Patent Office notes that claim 8 is drawn to a computer program product comprising a computer readable medium. The instant amendment addresses this issue, as claims 53 and 57, after entry of the instant amendment, are drawn to computer program products in a computer readable medium. Accordingly, this objection should be withdrawn.

Issues under 35 U.S.C. §102(b) and §103(a) in view of Wallace

Claims 2 to 14, 16 to 20, 22 and 44 to 60 stand rejected under 35 USC §102(b) as allegedly anticipated by, or, in the alternative, under 35 USC §103(a) as allegedly unpatentable over Wallace, et al. (1996) Protein Science 5:1001-1013 (hereinafter "Wallace").

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

In responding to Applicants' earlier comments regarding Wallace, the Patent Office notes that while Applicants' argument is based on the assertion that nothing in Wallace suggests that a functional site descriptor can be represented by non-catalytic backbone atoms, the instant claims are not drawn to "catalytic" or "non-catalytic" atoms.

The Patent Office further notes that while Applicants argue that Wallace does not suggest that a functional site descriptor incorporates one or more non-functional backbone atoms, incorporation of one or more non-catalytic functional backbone atoms is not a limitation of the instant claims.

To clarify the claimed invention, and to address this issue, claims 45, 53, 54, 56 and 57 are amended such that at least one of the atoms of substeps (b)(i), (b)(ii) or (b)(iii) comprises a backbone atom or backbone pseudoatom. In contrast, the atoms identified by Wallace were the catalytic oxygen atoms of the Scr and Asp side chains of the protein α-lytic proteinase 1lpr, as explained at page 10, lines 3-20, of the instant specification.

As Wallace does not teach inclusion of non-functional, i.e., non-catalytic, atoms in any 3D template, let alone a functional site descriptor according to the invention. Applicants respectfully submit that since, Wallace does not teach each and every limitation of the claimed

invention, it cannot anticipate Applicants' invention. Accordingly, this rejection can be properly withdrawn.

Claims 2 to 14, 16 to 20, 22 and 44 to 60 also stand alternatively rejected under section §103(a) as allegedly unpatentable over Wallace. No secondary reference to cure the defect in Wallace is cited. The Patent Office alleges that while Wallace does not specifically mention usage of a computer to implement the described method of searching structural databases, it would have been *prima facie* obvious to one of skill in the art at the time the invention was made to use a computer to practice the methods of Wallace.

Applicants respectfully submit that because Wallace fails to teach each and every limitation of the claimed invention (as demonstrated above), it clearly can not anticipate the use of a functional site descriptor according to the invention by any mode, computer or otherwise. As such, this rejection under section 103 can be properly withdrawn.

Issues under 35 U.S.C. §102(b) in view of Holm

The rejection of claims 2 to 14, 16 to 20, 22 and 44 to 60 under 35 USC §102(b) as anticipated by Holm, et al. (1997) PROTEINS: Structure, Function and Genetics 28:72-82, also has been maintained (hereinafter "Holm").

As is the case with Wallace, Applicants respectfully maintain that Holm does not teach each and every element of Applicants' claimed invention, as explained below.

Put simply, Holm does not teach or suggest functional site descriptors based on a combination of amino acid identity constraints and geometric constraints for particular atoms of several different amino acids, as is required by the instant claims. Instead, the purported global structural conservation patterns reported by Holm focused on global structural alignments of entire proteins. Holm's approach was reported to reveal a common structural core consisting of an ellipsoidal $(\beta\alpha)8$ barrel with a conserved metal ion binding site at the C-terminal end of strands $\beta1$, $\beta5$, $\beta6$, and $\beta8$ of specific urease, phosphotriesterase, and adenosine deaminase proteins (Holm, page 72, right hand column) aligned using the Dali program (id., page 73, left hand column). Clearly, such a motif is not a functional site descriptor based on amino acid identities and geometric constraints for particular atoms of several different amino acids. Accordingly, Holm cannot properly be said to anticipate the instant invention, as it fails to

disclose each and every aspect of the instant claims. For this reason, this rejection should also be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner should withdraw the rejection of the pending claims under 35 U.S.C. §101, 35 U.S.C. §112, second paragraph, 35 U.S.C. §102(b) and 35 U.S.C. §103(a). Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants respectfully request an interview with the Examiner before the first examination on the merits for this RCE. However, if the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

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Gregory F. Einhorn
Reg. No. 38,440

Fish & Richardson P.C.
4350 La Jolla Village Drive, Suite 500
San Diego, California 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099

Email gregory.einhorn@fr.com

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant : Skolnick et al. Art Unit : 1631
Serial No. : 09/322,067 Examiner : Dr. Michael Borin
Filed : May 27, 1999
Title : METHODS AND SYSTEMS FOR PREDICTING PROTEIN FUNCTION

In The Claims:

Claim 45 has been amended as follows:

45. (Twice amended) A computer program product comprising a computer useable medium having computer program logic recorded thereon for creating a functional site descriptor for use in predicting a biological function of a protein, said computer program logic comprising computer program code logic configured to perform the operations of:

(a) determining a set of geometric constraints for a functional site associated with a biological function of a protein, wherein a set of geometric constraints comprises one or more geometric constraints between at least three different atoms, wherein each atom is in a different amino acid residue of the protein and the different atoms comprise:

(i) an atom of a first amino acid residue of the functional site comprising the amino acid residue of part (a), wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon;

(ii) an atom of a second amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon; and[,]

(iii) an atom of a third amino acid residue of the protein, wherein the atom is selected from the group consisting of a backbone atom, a side chain atom, and a pseudoatom,

wherein at least one of (i), (ii) or (iii) comprises a backbone atom or a backbone pseudoatom;

(b) modifying one or more geometric constraints of said set of geometric constraints to produce a modified set of geometric constraints,

(c) comparing said modified set of geometric constraints to a data set of functional sites correlated with said biological function to determine whether said modified set of geometric constraints compares positively with said data set of functional sites correlated with said biological function and, if there is a positive correlation[:]; and,

(d) repeating said modifying and comparing operations of steps b and c to modify one or more of said geometric constraints of said set of geometric constraints to an extent that said modified set of geometric constraints compares positively with said data set of functional sites correlated with said biological function without encompassing a predetermined amount of data sets not correlated with said biological function.

Claim 53 has been amended as follows:

53. (Amended) A computer program product in a computer readable medium encoding a functional site descriptor, wherein the functional site descriptor defines at least one functional site of a protein, other than a divalent metal ion binding site, the functional site descriptor comprising:

(a) an amino acid residue identity constraint for a first amino acid residue of the functional site, wherein the first amino acid residue is identified as a single amino residue or as a subset of amino acid residues; and[,]

(b) one or more geometric constraints between at least three different atoms, wherein each atom is in a different amino acid residue of the protein and the different atoms comprise:

(i) an atom of the first amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon;

(ii) an atom of a second amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon; and[,]

(iii) an atom of a third amino acid residue of the protein, wherein the atom is selected from the group consisting of a backbone atom, a side chain atom, and a pseudoatom,

wherein at least one of (i), (ii) or (iii) comprises a backbone atom or a backbone pseudoatom.

Claim 54 has been amended as follows:

54. (Amended) A computer implemented method for determining a functional site descriptor that defines a spatial configuration of a functional site, wherein the functional site descriptor defines a functional site of a protein other than a divalent metal ion binding site, the method comprising the following steps:

(a) identifying an amino acid residue identity constraint for a first amino acid residue of the functional site, wherein the first amino acid residue is identified as a single amino residue or as a subset of amino acid residues; and[,]

(b) identifying one or more geometric constraints between at least three different atoms, wherein each atom is in a different amino acid residue of the protein and the different atoms comprise:

(i) an atom of the first amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon;

(ii) an atom of a second amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon; and[,]

(iii) an atom of a third amino acid residue of the protein, wherein the atom is selected from the group consisting of a backbone atom, a side chain atom and a pseudoatom,

wherein at least one of (i), (ii) or (iii) comprises a backbone atom or a backbone pseudoatom, thereby determining a functional site descriptor.

Claim 56 has been amended as follows:

56. (Amended) A computer-implemented method for defining a functional site descriptor of a protein comprising the following steps:

(a) identifying an amino acid residue identity constraint for a first amino acid residue of the functional site, wherein the first amino acid residue is identified as a single amino residue or as a subset of amino acid residues; and[,]

(b) identifying one or more geometric constraints between at least three different atoms, wherein each atom is in a different amino acid residue of the protein and the different atoms comprise:

(i) an atom of the first amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon;

(ii) an atom of a second amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon; and[,]

(iii) an atom of a third amino acid residue of the protein, wherein the atom is selected from the group consisting of a backbone atom, a side chain atom, and a pseudoatom,

wherein at least one of (i), (ii) or (iii) comprises a backbone atom, thereby [determining a] defining the functional site descriptor.

Claim 57 has been amended as follows:

57. (Amended) A computer program product in a computer readable medium for defining a functional site descriptor of a protein comprising a computer useable medium comprising a computer readable program code embodied therein, wherein the computer program product is capable of defining a functional site descriptor of a protein by a process comprising the following steps:

(a) identifying an amino acid residue identity constraint for a first amino acid residue of the functional site, wherein the first amino acid residue is identified as a single amino residue or as a subset of amino acid residues; and[,]

(b) identifying one or more geometric constraints between at least three different atoms, wherein each atom is in a different amino acid residue of the protein and the different atoms comprise:

(i) an atom of the first amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon;

(ii) an atom of a second amino acid residue of the functional site, wherein the atom is selected from the group consisting of a backbone amide nitrogen, an alpha-carbon, a backbone carbonyl carbon, a backbone carbonyl oxygen, a backbone pseudoatom, and a beta-carbon; and[,]

(iii) an atom of a third amino acid residue of the protein, wherein the atom is selected from the group consisting of a backbone atom, a side chain atom, and a pseudoatom,

wherein at least one of (i), (ii) or (iii) comprises a backbone atom or a backbone pseudoatom, thereby [determining a] defining the functional site descriptor.